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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/089,514	03/29/2002	Koji Yanai	2002_0451A	7814

EXAMINER
KERR, KATHLEEN M

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/089,514	YANAI ET AL.	
	Examiner	Art Unit	
	Kathleen M Kerr	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *23-25 and 28-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22,26 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/15/02, 3/29/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *KEGG enzyme*.

DETAILED ACTION

Application Status

1. In response to the previous Office action, a written restriction requirement (mailed on October 7, 2004), Applicants filed an election received on November 5, 2004. Claims 1-31 are pending in the instant Office action.

Election

2. Applicant's election with traverse of Group I, Claims 1-22 ad 26-27 as they relate to SEQ ID NO:1 in the reply filed on November 5, 2004 is acknowledged. The traversal is on the ground(s) that Groups I-III are inseparable because all three genes are required to be transformed into the claimed transformant. This is not found persuasive because only a single gene is required to be transformed. The claim language clearly sets forth that "the transformant is transformed by introducing **a gene** involved in a biosynthetic pathway from chorismic acid to p-aminophenylpyruvic acid" (emphasis added). The functional limitations do not require that the other two genes, as noted by Applicant, be transformed into the claimed organism. Applicant also argues that it would not be unduly burdensome to search the three SEQ ID NOs in Groups I-III. This argument is not persuasive because the restriction is set forth under 35 U.S.C. § 121 and 372, which do not require a showing of burdensome search (that is U.S. practice)

The requirement is still deemed proper and is therefore made FINAL. Claims 1-31 are pending. Claims 23-25 and 28-31 are withdrawn from consideration as non-elected inventions. Claims 1-22 and 26-27 will be examined herein.

Priority

3. The instant application is granted the benefit of priority for International Application No. PCT/JP00/06783 filed on September 29, 2000 as requested in the declaration. The instant application is granted the benefit of priority for the foreign application 11/276314 filed on September 29, 1999 in Japan as requested in the declaration.

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. § 119(a)-(d). The certified copy has been filed in the international application; said copy is not in English and, thus, cannot be used to support an earlier effective filing date. No translation is required unless prior art rejections must be overcome.

Information Disclosure Statement

4. The information disclosure statements filed on March 29, 2002 and May 15, 2002 have been reviewed, and their references have been considered as shown by the Examiner's initials next to each citation on the attached copies.

Compliance with the Sequence Rules

5. By virtue of the filing of a sequence listing of 23 sequences in computer readable form and paper copy on April 30, 2002, the instant application fully complies with the sequence rules.

Objections to the Specification

6. In the specification, the Abstract is objected to for not completely describing the disclosed subject matter (see M.P.E.P. § 608.01(b)). It is noted that in many databases and in foreign countries, the Abstract is crucial in defining the disclosed subject matter, thus, its completeness is essential. The Examiner suggests the inclusion of the full name of the enzymes

for papA, papB, and papC as described on page 12 of the specification and the source species of said enzymes, *Streptomyces venezuelae*, used in the specification for completeness.

7. The specification is objected to for being unclear in its examples. On page 14, lines 4-6, "Streptomyces loidens" is misspelled; the correct spelling is ---loidensis--- as found in USPN 2,990,325. The nature of "Nocardia parafinnica" is wholly unclear as it cannot be identified in the prior art whatsoever. The term "corynesin" is misspelled; the correct spelling is ---corynecin--- as found in USPAP 20020072062, for example, and in non-patent literature publications of the 1970's.

8. The specification is objected to for a typographical error. On page 14, line 12, the citation's date is 1997 (not 1977 as shown). Correction is required.

Claim Objections

9. Claim 6 is objected to for having a punctuation error. The period after "formula" is premature since the formula must be included in the single-sentence claim.

10. Claim10-22 are objected to under 37 C.F.R. § 1.75(c) as being in improper form because a multiple dependent claim cannot depend from another multiple dependent claim. See M.P.E.P. § 608.01(n).

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 1-7, 18-20, and 22 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "a gene involved in a biosynthetic pathway from chorismic acid to p-aminophenylpyruvic acid" (emphasis added) is unclear. No specific pathway is identified in the prior art. The specification on page 12 identifies the following enzymes as examples or enzymes involved, 4-amino-deoxychorismic acid synthase (papA), 4-amino-deoxychorismic acid mutase (papB), and 4-amino-deoxyprephenic acid dehydrogenase (papC); however, such examples cannot be read as real limitations into the specification. Moreover, the article "a" indicates that more than one biosynthetic pathway is within the claimed limitations; the nature of such a pathway distinct from the enzymes noted on page 12 is wholly unclear. Thus, the nature of the genes/enzymes within the metes and bounds of the claimed limitation is unclear. Clarification is required.

12. Claims 1-7, 18-20, and 22 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "(biosynthesis gene)" as it appears in parentheses is wholly unclear in Claim 1. While the antecedent basis in Claims 8-9 is clear, the use of parentheses in Claim 1 is unclear. Clarification is required.

13. Claims 2, 3, 8-18 and 22 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The nature of the secondary metabolite produced in the microorganism is wholly unclear, as it needs to be biosynthesized "via chorismic acid". The limitation of this phrase is unclear as to its metes and bounds. What link must "via" require? This is not a term of art. Moreover, the phrase "synthesized from at least one building block" in Claim 3 is also unclear. It does not clarify the issue with the language of Claim 2, and it further confuses the term as to how it may further limit. Clarification is required.

14. Claims 5, 8-18 and 22 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The nature of the secondary metabolite produced in the microorganism is wholly unclear as it needs to be "synthesized from at least one building block", which phrase is unclear. It confuses the term as to how it may further limit. Clarification is required.

15. Claims 8-15, 17-20 and 22 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In Claims 8-9, "**a** gene" (emphasis added) is required to be introduced; however, three open reading frames, i.e., three genes, are required to be used. Clarification on this discrepancy is required.

Additionally, the nature of the synthase, mutase, and dehydrogenase genes required is unclear. In the instant specification, *S. venezuelae* genes are taught as papA (synthase), papB

(mutase) and papC (dehydrogenase) (see page 3 and the Examples). These genes are analogous to those taught by Blanc *et al.* (1997) (see IDS) who first ascribe these gene names and functions (see page 196, right column). The gene papA is, however, distinct from the following mentioned on page 12:

In *E. coli*	Kaplan *et al.* teach pabA and Goncharoff *et al.* teach pabB.
In *B. subtilis*	Slock *et al.* teach pab and pabC.
In *K. pneumoniae*	Kaplan *et al.* teach pabA and Goncharoff *et al.* teach pabB.
In *S. venezuelae*	Brown *et al.* teach pabAB
In *S. cerevisiae*	Edman *et al.* teach pabAB.

What additionally lacks clarity is that Blanc *et al.* teach that papA resembles pabAB (see page 196, left column). Thus, the nature of the synthase gene to be used in the instant claims is wholly unclear based on indications from the specification. With the specification teaching papA, papB, and papC and trying to equate papA with pabA, pabB, pab, and/or pabC from the art, the nature of the enzyme is wholly unclear. Moreover, the enzyme 4-amino-4-deoxychorismate synthase is known as E.C. 6.3.5.8 with optional gene names of pabA and pabB (see attachment). While the catalytic activity is clearly described (see page 12), the nature of the synthase is wholly unclear in view of the art and the disclosure.

The mutase (papB) and dehydrogenase (papC) genes are only related specifically to those in Blanc *et al.* (see page 14). These enzymes are not found in the E.C. database. Blanc *et al.* related them to TyrA and PheA, but this limitation cannot be read into the claims. While the catalytic activities are clearly described for these two enzymes(see page 12), the nature of the mutase and the dehydrogenase is wholly unclear having only Blanc *et al.* and the instant disclosure to support the enzymatic activity.

16. Claim 20 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "**a** strain PF1022 deposited ... under accession number of FERM BP-7255" (emphasis added) is unclear. The article "a" indicates any strain of PF1022; however, a specific strain is later noted by accession number. Thus, it is unclear if the strain used in a species or genus. Clarification is required.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

17. Claims 1-16, 18-20, 22 and 26 are rejected under 35 U.S.C. § 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The instant claims are drawn to transformants comprising a polynucleotide (or the polynucleotide itself) wherein the polynucleotide is claimed solely by function and without any structural limitations.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as be structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." University of California v. Eli Lilly and Co., 1997 U.S. App. LEXIS 18221, at *23, quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed.

Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these.

In the instant specification, genes encoding a synthase (papA), mutase (papB), and dehydrogenase (papC) of the claimed invention are described from *S. venezuelae* (SEQ ID NOs:1-6); the prior art teaches analogous genes from *S. pristinaespiralis* (see Blanc *et al.*). In the instant claims, these genes are only described by function; no structural relationship is described or used in the claims. Thus, one of skill in the art would be unable to predict the structure of other members of this genus by virtue of the instant disclosure.

For Claims 1-7, 18-20 and 22, the enzyme name is not even a limitation. Said claims are drawn to *any* gene encoding a protein involved in a biosynthetic pathway from chorismic acid to p-aminophenylpyruvic acid. In addition to the lack of clarity as noted above, the genus is very broad in the absence of a limiting enzyme function. While the specification contains species of the claimed genus, said species do not adequately represent the claimed genus because no correlation between the structure of SEQ ID NOs:1-6 and this broad function is described.

For Claims 8-16 and 26, an enzyme name is a claim limitation but no specific structure is required. The Examiner notes that said claims are drawn to "the amino acid sequence of SEQ ID NO:2 or a **modified** sequence of SEQ ID NO:2 having 4-amino-4-deoxychorismic acid synthase

activity" (see Claim 10, for example) wherein said modification is defined as one or more substitutions, deletions, insertions, or additions (see page 13), which definition is essentially limitless on the amount of modification to the named structure of SEQ ID NO:2. Since this enzyme name lacks clarity (see above) and does not garner a particular structural feature as based on the art, the enzyme name cannot support both a structural and functional limitation for the product of the claimed invention. The Examiner notes that Claims 17 and 27 are excluded from the instant rejection since exact structure for the genes encoding the enzymes is required.

For Claim 9 wherein the genes must be from *Streptomyces*, *Nocardia*, or *Corynebacterium*, the Examiner notes that only two species of *Streptomyces* are described and these do not represent the claimed genus of all *Streptomyces* papA, papB, and papC genes because no structure/function correlation has been described within said genus. No species of *Nocardia* or *Corynebacterium* has been described, thus these genus limitations wholly lack adequate written description.

18. Claims 6-18 and 22 are rejected under 35 U.S.C. § 112, first paragraph, written description, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 6 is drawn to a transformant that can produce a particular metabolite that is claimed solely by function and without any structural limitations on the transformant.

The Court of Appeals for the Federal Circuit has recently held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as be structure, formula [or] chemical name,' of the claimed subject

matter sufficient to distinguish it from other materials." University of California v. Eli Lilly and Co., 1997 U.S. App. LEXIS 18221, at *23, quoting Fiers v. Revel, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original). To fully describe a genus of genetic material, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecules, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these.

In the instant specification, a single microorganism is described as producing PF1022 as found in Claim 6. No description in the specification or the art identify the biosynthetic pathway of said compound thus the structural features that garner this function of the microorganism are unknown. Thus, one of skill in the art would be unable to predict the structure of other members of this genus by virtue of the instant disclosure.

For Claim 22 as it depends from Claims 6 or 7, no species of the claimed genus (plant making PF1022) is described. Without a representative species, the claimed invention wholly lacks adequate written description.

19. Claims 1-22 are rejected under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for transformants of *Mycelia sterilia* containing genes encoding SEQ ID NOs: 2, 4, and 6 that make para-substituted PF1022 wherein the substitution is a $-NO_2$ or $-NH_2$ functional group, does not reasonably provide enablement for any transformant to make any para-substituted metabolite with any nitrogen-containing functional

group using any genes. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. To make the claims to the full extent of their scope would require undue experimentation.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

The instant specification teaches the identification of papA, papB, and papC genes in *Streptomyces venezuelae* as found in the vicinity of the known gene pabAB. The pabAB encodes p-aminobenzoic acid synthase; the papA, papB, and papC genes are described as

encoding a synthase, a mutase, and a dehydrogenase, respectively (see both Blanc *et al.* and the instant specification) and such activities are distinct from that of pabAB. The papA, papB, and papC genes are described as being analogous to papA, papB, and papC genes from *S. pristinaespiralis*, which microorganism naturally produces pristinamycin - a secondary peptide metabolite containing a benzene ring with a para-substituted group that is a nitrogen-containing group (see Blanc *et al.*).

The instant inventors use the papA, papB, and papC genes in a fungus that produces PF1022 (called *Mycelia sterilia* and *Rosellinia sp.* PF1022 in the art) to produce $-NO_2$ and $-NH_2$ -para-substituted PF1022 analogs (see Figure 13). These analogs are produced due to the incorporation of the newly produced p-amino-D-phenyllactate that is incorporated into PF1022 in place of D-phenyllactate that is incorporated natively (see Yanai *et al.* 2004, Figure 2). Thus, the teachings of the instant specification enable the production of metabolite analogs wherein the native metabolite incorporates phenyllactate and wherein $-NO_2$ or $-NH_2$ analogs are produced using host cells transformed with papA, papB, and papC genes. However, due to the specificity of biosynthetic enzymes, which specificity is well know in the art, other analogs are not enabled and the use of other genes (even the identification of other genes) is not enabled. While one of skill in the art may be able to *find* other papA, papB, and papC genes using hybridization techniques and a knowledge of organisms that may produce/use p-aminophenylpyruvate (the product of the papA-papB-papC pathway), this does not enable one of skill in the art to *make* such genes for use in the claimed transformants because the relevant characteristics of these genes and/or the enzymes they encode so that their functional properties are maintained are unknown. The predictability of the ability of papA, papB, and papC enzymes to incorporate any

nitrogen-containing functional group in the para position of any secondary metabolite is very, very low.

20. Claims 20 and 21 are rejected under 35 U.S.C. § 112, first paragraph, enabling deposit, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. To produce the claimed transformants, one of skill in the art is required to have FERM BP-2671 or FERM BP-7255. While the instant specification contains deposit information, the requirements to enable such a deposit have not been fully met by the instant application because the record must also contain a statement certifying that all restrictions on accessibility to said deposit be irrevocably removed by Applicant upon the granting of the patent (see M.P.E.P. § 2404.01); this statement may be certified by Applicants or Applicants' representative.

Claim Rejections - 35 U.S.C. § 101

35 U.S.C. § 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

21. Claims 26-27 are rejected under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter. Claims 26-27, as written, do not sufficiently distinguish over cells as they naturally exist because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered

non-statutory subject matter. See Diamond v. Chakrabarty, 447 U.S. 303, 206, USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g. by insertion of "isolated" or "purified" provided that support can be found in the specification for such an amendment. See M.P.E.P. § 2105.

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

22. Claims 1-5 and 18 are rejected under 35 U.S.C. § 102(b) as being anticipated by Blanc *et al.* The instant claims are drawn to microorganisms that produce peptides as secondary metabolites wherein said microorganisms are transformed with papA encoding 4-amino-4-deoxychorismic acid synthase and now produce secondary metabolites with a nitrogen-containing functional group at the para position of a benzene ring in the metabolite.

Blanc *et al.* teach SP210::pVRC414-1 that produces pristinamycin in the presence of DMPAPA or MMPAPA (see page 195, left column). Blanc *et al.* also teach transforming said strain with the papA gene in pIJ903 (see page 195, left column), wherein papA encodes 4-amin-4-deoxychorismic acid synthase (see page 196, right column); said transformant produces para-aminobenzoic acid (see page 195, left column), which contains a nitrogen-containing functional group at the para position.

23. Claim 26 is rejected under 35 U.S.C. § 102(b) as being anticipated by Blanc *et al.* The instant claims are drawn to polynucleotides encoding an enzyme having 4-amino-4-deoxychorismic acid synthase activity.

Blanc *et al.* teach the papA gene of *Streptomyces pristinaespiralis*, which encodes 4-amino-4-deoxychorismic acid synthase (see abstract and page 196, right column).

Additionally Cited Art

24. The Examiner makes the following of record:

a) Yanai *et al.* Para-position derivatives of fungal anthelmintic cyclodepsipeptides engineered with *Streptomyces venezuelae* antibiotic biosynthetic genes. Nature Biotechnology (2004) 22(7): 848-855. Yanai *et al.* is not prior art.
b) Brown *et al.* (see IDS) teach a pabAB gene from *S. venezuelae* that is 86% identical to SEQ ID NO:1 encoding a protein that is 88% identical to SEQ ID NO:2 (see attached alignments using GenBank Accession Numbers U21728 and AAB30312.1); the function of said protein is not 4-amino-4-deoxychorismic acid synthase but p-aminobenzoic acid synthase and, thus, not prior art on Claim 26.
c) He *et al.* teach a *Streptomyces* venezuelae chloramphenicol biosynthetic gene cluster (see also GenBank Accession Number AF26220); the N-terminus of said cluster being 86% identical to SEQ ID NO:1 (see attached alignment). He *et al.* do not describe this portion of the cluster as encoding a protein despite the fact that this portion is identical to that described by Brown *et al.* as noted above. He *et al.* is not prior art.
d) Miyadoh *et al.* teaches that the sterile mycelium fungal strain that produces PF1022 (referred to in the instant specification and the prior art as *Mycelia sterilia*, which is not an official taxonomic strain) should be taxonomically known as *Rosellinia sp.* PF1022. Thus, the Examiner makes clear that *Mycelia sterilia* and *Rosellinia sp.* PF1022 are the same strain.

Conclusion

25. Claims 1-22 and 26-27 are rejected for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kathleen M Kerr whose telephone number is (571) 272-0931. The examiner can normally be reached on Monday through Friday, from 9:00am to 6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathupura Achutamurthy can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Kathleen M Kerr
Primary Examiner
Art Unit 1652

January 21, 2005